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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,344	07/16/2001	Wenfang Chen	P50892	2762

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EXAMINER
MAYER, SUZANNE MARIE

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 06/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/889,344	CHEN ET AL.	
	Examiner	Art Unit	
	Suzanne M. Mayer	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28 and 35-38* is/are pending in the application.

4a) Of the above claim(s) *30-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8, 12-14, 21-27, 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group 1, claim(s) 1-29 and 35-38, drawn to a method of screening candidate compounds using proteins that interact with SEQ ID NO:1.

Group 2, claim(s) 30-34, drawn to a biotinylation reagent.

The inventions listed as Groups 1 and 2 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: a method of screening candidate compounds and a novel biotinylation reagent constitute two unique inventive concepts.

2. During a telephone conversation with Mr. Edward Gimmi on 12 May, 2004 a provisional election was made without traverse to prosecute the invention of Group 1, claims 1-29 and 35-38. Affirmation of this election must be made by applicant in replying to this Office action. Claims 30-34 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 6, and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is rejected as it is unclear what Applicant means and regards as 'genetic engineering' as this term can mean anything from altering a single nucleotide base of a gene to inserting mouse genes into maize.

Claim 26 is rejected because exactly what defines a crude protein is unclear. A crude protein mixture or crude extract containing a particular protein is intended to mean a protein with a considerable amount of other proteins in the mixture. However, what an individual crude protein consists of has no art-accepted meaning.

Claim Rejections - 35 USC § 103

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claims 1-8, 12-14, 21-25, 27 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cappello, in view of Gorman et al.

Cappello teaches a method of labeling beta-casein by reacting factor XIIIa, a well known transglutaminse, with 5-biotinamidopentylamine (BAPA) and detecting the incorporation of this label into beta-casein with a candidate compound of streptavidin. The reaction is carried out in a 96 well microtiter plate. Cappello does not, however, teach the specific amino acid sequence essential for this reaction and labeling to occur.

Gorman et al. teach that the primary site of factor XIIIa incorporation into beta-casein is the amino acid Gln-167. This amino acid had been identified by using a 15 amino acid synthetic peptide where the sequence was derived from the primary amino acid sequence of beta-casein and corresponding to amino acids 161-175, the sequence being –SVLSLS*QSKVL*PVPE-. Further characterization of this synthetitic peptide showed certain aliphatic hydrophobic amino acids were essential to the specificity and reaction with factor XIIIa. By altering the peptide –SVLSLS*QSKVL*PVPE- with single amino acid substitutions of a glycine residue at various locations, specifically at Leu-163 (e.g., SV***G***SLS*QSKVL*PVPE) or Val-170 (e.g., SVLSLS*QSKGL*PVPE) or Leu-171 (e.g., SVLSLS*QSKVG*PVPE), these altered peptides showed a considerable decrease in specificity for factor XIIIa. No change in specificity was seen for glycine substitutions at positions of 162, 166 or 173. Therefor, Gorman et al. teach not only that Gln-167 is essential, but also that aliphatic hydrophobic amino acids such as the two in the sequence -QSKVL- are essential for the specificity of transglutaminases.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the sequence from beta-casein, as taught by Gorman et al., and to use the sequence that had been identified as being responsible for the reaction with transglutaminases in an experiment similar to that described by Cappello. Gorman et al. do not specifically define the minimal sequence smaller than the 15 amino acids of beta-casein 161-175 SVLSLS*QSKVL*PVPE that are absolutely essential. However, the glycine substitution experiments which were carried out revealed that certain aliphatic hydrophobic amino acids were essential. Thus, one of ordinary skill in the art would be able to figure out which exact amino acids from the above 15 amino acid sequence were essential using only routine experimentation.

Claims 12-14 are included in this rejection because Cappello performed his experiments in a 96 well mictrotiter plate. It would have been obvious to one of ordinary skill in the art at the time the invention was made to reproduce this and to additionally perform these experiments in plates with wells of larger sizes such as 384 and 1536 since no patentable distinction is seen.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1, 12, 21, 27 and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Cappello (WO 9523611), as evidenced by Gorman et al.

Cappello discloses in Example 5, pp. 49-51, a method of analyzing a purified protein, PPAS1-A, to assess its ability to act as a substrate factor XIIIa. The experiment was performed on a standard 96-well microtiter plate and as a positive control, beta-casein was used as a substrate for factor XIIIa, which contains the sequence –QSKVL- (amino acids 167-171), and because it is well known in the art to be a very good substrate for factor XIIIa. Gorman et al. disclose that the primary site of factor XIIIa-catalyzed amine incorporation in beta-casein is glutamine 167 (Gorman et al., p. 2713, 1st column, last paragraph) which was identified by using a 15 amino acid synthetic peptide derived from the primary amino acid sequence of beta-casein corresponding to amino acids 161-175 (SVLSLS*QSKVL*PVPE). The Capello experiment was performed as follows: PPAS1-A and beta-casein were reacted with factor XIIIa and the detectable labeling compound 5-biotinamidopentylamine (BAPA). The labeled proteins were then reacted with another candidate compound, streptavidin, which binds with high affinity to BAPA. If incorporation of the labeling compound has occurred in PPAS1-A and beta-casein, then it will be detected when/if streptavidin binds to the BAPA which induces a color change if successful incorporation of the labeling compound has occurred. A color change was seen in the wells for both PPAS1-A and beta-casein indicating BAPA incorporation in both proteins.

Beta-casein, as is known in the art, contains the sequence –QSKVL- (see Gorman et al., which is the basis of the claims 1, 12, 21, 27 and 29. While the examiner

acknowledges the applicants claim 'A modified protein containing the sequence QSKV(L or I).....', for purposes of this claim rejection a modified protein containing this sequence is considered to be functionally equivalent to a protein already containing this sequence.

9. Claim 1 is rejected because the experiment carried out by Cappello meets the limitations of claim 1 as described above. Claim 12 is rejected because the experiment took place in a 96 well microtiter plate. Claim 21 is rejected because, as Gorman et al. teach the site of the reaction for a transglutaminase (Factor XIIIa) with beta-casein and a labeling compound is at the glutamine of residue 167. Furthermore, this glutamine site corresponds to the amino acid sequence 167-171, -QSKVL- (p. 2713, 1st column last paragraph). Therefore, Cappello, as evidenced by Gorman et al., anticipates claim 21. Claim 27 is rejected as being anticipated by Cappello as 5-biotinamidopentylamine (BAPA) is a biotin label. Claim 29 is rejected because in Example 5 of Cappello (pp. 51, lines 13-18), a color change was seen in the wells for beta-casein indicating the labeling compound BAPA was successfully incorporated.

Conclusion

10. Claims 1-8, 12-14, 21-27, and 29 are rejected. Claims 9-11, 15-20, 28, 35-38 are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suzanne M. Mayer, Ph.D. whose telephone number is

571-272-2924. The examiner can normally be reached Monday-Friday from 9.00am-5.30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SMM
2 June, 2004

ROBERT A. WAX
PRIMARY EXAMINER